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PATENT
Attorney Docket No.: 02307E-085110US
Client Ref. No.: 98-035-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Zuker *et al.*

Application No.: 09/463,733

Filed: June 12, 2000

For: METHOD FOR MODULATING G-PROTEIN COUPLED RECEPTORS

Examiner: Carla J. Myers

Art Unit: 1656

AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office Action mailed February 27, 2002, please amend the above-identified application as set forth below. Enclosed herewith is a fee authorization to extend the time for response for three months from May 27, 2002 to August 27, 2002.

IN THE CLAIMS:

Please cancel claims 2, 18, and 21 without prejudice to subsequent revival. Please replace claims 1, 15, 24, and 33 with the following clean copies of the amended claims. A marked up version showing the amendments is provided in Appendix A, attached hereto.

B1

1. (twice amended) A method of screening *in vitro* for modulators of G-protein coupled receptor signal transduction, the method comprising the steps of:

(i) providing a sample comprising a G-protein coupled receptor and a recombinant RDGC phosphatase;

(ii) contacting the sample with a test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity; and

(iii) detecting a change in the level of RDGC GPCR phosphatase activity in the sample in comparison to the level of activity in the absence of the test compound, thereby detecting a modulator of G protein coupled receptor signal transduction.

B2

15. (twice amended) A method of screening a cell for modulators of G-protein coupled receptor signal transduction, the method comprising the steps of:

(i) providing a cell sample comprising rhodopsin and RDGC phosphatase;

(ii) contacting the sample with a test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity; and

(iii) detecting a change in the level of RDGC GPCR phosphatase activity in the sample in comparison to the level of activity in the absence of the test compound, thereby detecting detecting a modulator of G protein coupled receptor signal transduction.

B3

24. (twice amended) A method of screening *in vivo* for modulators of G-protein coupled receptor signal transduction, the method comprising the steps of:

(i) providing an animal comprising a cell comprising a G-protein coupled receptor and an RDGC phosphatase;

(ii) contacting the animal with a test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity; and

B3 cont'd

(iii) detecting a change in the level of RDGC GPCR phosphatase activity in the animal in comparison to the level in the absence of the test compound, thereby detecting a modulator of of G protein coupled receptor signal transduction.

B4

33. (twice amended) A method of screening *in vivo* for modulators of G-protein coupled receptor signal transduction, the method comprising the steps of:

(i) providing an animal comprising a cell comprising rhodopsin and RDGC phosphatase;

(ii) contacting the animal with a test compound suspected of having the ability to modulate RDGC GPCR phosphatase activity; and

(iii) detecting a change in the level of RDGC GPCR phosphatase activity in the animal in comparison to the level in the absence of the test compound, thereby detecting a modulator of of G protein coupled receptor signal transduction.

REMARKS

With entry of the current amendment, claims 1, 15, 24, and 33 have been amended and claims 2, 18, and 21 have been cancelled. Claims 1, 3-17, 19, 20, and 22-38 are therefore pending in the application. A copy of the currently pending claims is provided in Appendix B, attached hereto.

The amendments to the claims are fully supported in the specification and claims as filed.

Claims 1, 15, 24, and 33 have been amended to recite detecting a change in the level of activity in comparison to the level in the absence of the test compound. Support for the amendment can be found, for example, in the paragraph at page 22, line 26 through page 23, line 2.

The rejections are addressed in the order presented in the Office Action mailed February 27, 2002.

The invention

The invention is based on Applicants' discovery of the mechanistic basis of the site of action of RGDC phosphatase. RDGC phosphatase removes phosphate from GPCRs, *e.g.*, rhodopsin. Accordingly, modulators of RDGC phosophatase activity also modulate GPCR activity. The invention therefore provides a method of identifying modulators of GPCR-mediated signal transduction by identifying inhibitors and activators of RDGC phosphatase activity.

Rejection under 35 U.S.C. § 112, first paragraph

The claims were rejected as allegedly lacking adequate descriptive support in the specification. In particular, the rejection alleges that the specification does not disclose an adequate number of RDGC allelic variants, mutants, or homologs to convey to one of skill in the art that Applicants were in possession of the claimed invention. Further, the Examiner contends that the claims do not recite any structural properties of the RDGC proteins. Applicants respectfully traverse. Compliance with the written description requirement does not demand a listing of multiple species, but may also be met by identifying structural and functional characteristics of the genus. These characteristics are present in the claims.

Requirements for the written description of a chemical genus are set forth by the Federal Circuit in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). In *Lilly*, the Court stated that, "[a] description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs....*or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.*" (emphasis added) *Lilly*, 43USPQ2d at 1406. The Examiner contends that structural features are not recited in the claims. However, the specification teaches that RDGC phosphatases are known in the art. Indeed, the definition of RDGC phosphatase on page 8 includes the reference RDGC phosphatase sequence, *i.e.*, reference structure, taught by Steele *et al.* The definition also teaches that RDGC phosphatases have at least 60% identity to that reference sequence

and further, provides a definition of percent identity, which is readily determined by those in the art using well known algorithms (*see, e.g.,* the passage starting at page 18).

An adequate written description does not require a detailed description of that which is known to one of ordinary skill in the art. The Revised Written Description Examination Guidelines, Federal Register, Vol. 66, No.4, 1099, Jan. 5, 2001, indicate that

> What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. (page 1106)

Therefore, in light of the disclosure in the specification, taken together with that which is known in the art, the genus of RDGC phosphatases for use in the invention are defined by a structural feature that is a hallmark of the genus.

The genus is additionally described by the functional elements in the claims. The claims are drawn to methods of identifying modulators of RDGC activity. Accordingly, the RDGC phosphatases must be functional. This functional characteristic is fully supported by the description in the specification. Not only is the activity of RDGC phosphatase well known in the art (*see, e.g.,* the references indicated in the specification at page 3, lines 8-12), but the specification also provides descriptions of RDGC phosphatase activity assays, both direct (*see, e.g.,* page 12, lines 17-21, and page 25, line 31 through page 226, line 12) and indirect (*see, e.g.,* page 26 starting at line 13).

The claims thus set forth both structural and functional elements that are shared by the genus of RDGC phosphatases set forth in the claims. Accordingly, the invention is fully described and complies with the standards defined in *Lilly*. Applicants therefore respectfully request withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-36 were rejected as allegedly indefinite for failing to recite a final process steps that agrees back with the preamble. In order to expedite prosecution, the claims have been amended to recite a final step that agrees with the preamble. Applicants therefore respectfully request withdrawal of the rejection.

Claims 15-23 were rejected as allegedly indefinite because the claims recite an *in vivo* method, yet include a step of contacting a sample with a test compound. In order to expedite prosecution, claim 15 has been amended to recite a method of screening a cell and contacting a cell sample with the test compound. Applicants therefore respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 102

Claims 1, 3, 4, 6, 7, 12-14 were rejected as allegedly anticipated by Byk *et al.* Claim 1 has been amended to recite a recombinant RGDC phosphatase. Byk *et al.* do not disclose a recombinant phosphatase. Applicants therefore respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 103

Claims 1-38 were rejected as allegedly unpatentable over Byk *et al.* in view of Zuker (reference "AG") and Zuker (GenBank Accession NO. M17718, reference "AE"). The rejection alleges that it would have been obvious to have modified the method of Byk to use recombinant RDGC; and further, that in light of Zuker, it would have been obvious the use cells or transgenic organisms in the method of Byk instead of membrane preparations. Applicants respectfully traverse. In order to establish a proper *prima facie* case of obviousness, three basic criteria must be met: (i) the prior art must teach or suggest all of the claimed elements; (ii) there must be some suggestion or motivation to modify the reference or to combine reference teachings; and (iii) there must be a reasonable expectation of success. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior

art, not in applicant's disclosure. M.P.E.P. § 2143, *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The argument presented in the Office Action does not meet these requirements.

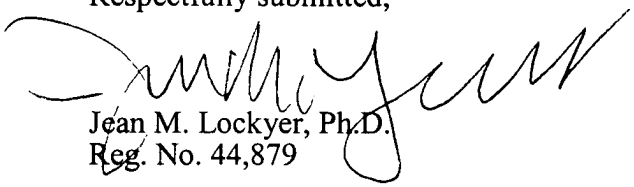
The current invention provides a method of screening for modulators of GPCR signal transduction. Although Byk *et al.* teach the analysis of *Drosophila* membranes to determine the phosphorylation and dephosphorylation states of arrestin and rhodopsin, the reference does not teach an *in vivo* analysis that establishes the direct role of RDGC phosphates in GPCR-mediated signal transduction. The rejection does not present evidence or reasoning as to why one of skill in the art would use RDGC phosphatases as a target to modulate GPCR-mediated signal transduction, in the absence of confirmation of the biological role of RDGC phosphatase. Thus, the argument does not establish a proper case of *prima facie* obviousness. Applicants therefore respectfully request withdrawal of the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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